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EVALUATION OF ANTI DIABETIC ACTIVITY OF ETHANOLIC EXTRACT OF ANDROGRAPHIS ELONGATE LEAVES

Aamir Khan Yusuf Khan*, Javariya Mubin Sayyada, Maliha Asif, Noor Ul Huda and Maryam Mehnaz

Department of Pharmacology Deccan School of Pharmacy, Dar-us-salam, Aghapura, Hyderabad. Telangana.

***Corresponding Author: Aamir Khan Yusuf Khan**

Department of Pharmacology Deccan School of Pharmacy, Dar-us-salam, Aghapura, Hyderabad. Telangana

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ABSTRACT

Andrographis elongate is having ethnomedicinal use for anti-diabetic activity. The ethanolic extract from whole plant of *Andrographis elongata* were subjected to preliminary phytochemical analysis which shown presence of flavonoids, alkaloids, Glycosides, tannins, proteins, steroids and phenol with absence of saponins and anthroquinones. The anti-diabetic activity of leaves of *Andrographis elongata* is evidenced byblood glucose level, estimation of lipid profile activity of *Andrographis elongata* and the evidentreduction in SGOT, SGPT in liver and creatinine in serum also proves that the *Andrographis elongata* reduced the Pancreas, liver damage which is common in diabetes.Thus, it may be concluded that *Andrographis elongata* produced significant antidiabetic activity in streptozotocin induced diabetic rats. The efficacy of the *Andrographis elongata* was comparable to that of Glibenclamide.

KEYWORDS: Anti-diabetic activity, *Andrographis elongate* leaves, Phytochemical Qualitative Analysis, wistar albino rats.

INTRODUCTION

Management of Diabetes mellitus is a global problem, successful treatment is very important for preventing or at least delaying the onset of long-term diabetic complications like diabetic neuropathy, nephropathy, retinopathy, erectile dysfunction, hypertension and injury caused by ischaemic and reperfusion.[1,2] Through nature in the form of herbal medicines or drugs with very minimal adverse effects are preferred when compared to the available synthetic drugs to treat such chronic disease and disorders.[3] Herbal drugs as therapeutic agents are a nature's boon when compared to the severe adverse effects of the allopathic medical practice for diabetes, despite the fact that the search for a complete and permanent cure for the disease is being pursued uncompromisingly by eluding physicians and researchers.[4] These herbal remedies which exemplifies the process of symbiosis still remains unfamiliar up to data technical advances, which has fashioned a marvelous scope for folk lore or traditional medicines.[5] It is supposed that the tradition medicines used for the treatment of diabetes mellitus satisfy the sequence of complication of the disease.

Even though, the traditional medicinal plants are used to cure the disease from human origin, scientific validation of such medicinal plants are necessary and also scientific research to prove its pharmacological and therapeutic efficacy is became vital.

Andrographis elongate is having ethnomedicinal use for anti-diabetic activity. As per the literature review no scientific method for anti-diabetic activity has been reported on this plant. Hence, this study has been taken to explore the anti-diabetic potential of Andrographis elongate on streptozotocin induced diabetes in Wister albino rat.

MATERIALS AND METHODS

Plant Collection and Identification

Fresh plant of *Andrographis elongata* was collected from the forest from chittur dist. The plant materials were identified and authenticated by Prof. Madhav Shetty, Dept. of botany, Taxonomist, SV University, Tirupati. A voucher was kept in the Department of Pharmacognosy for reference.

Preparation of plant extract

The sample was washed with distilled water to remove any adherent particles, shade dried and powdered. 25g of each sample was weighed and extracted with 300ml of ethanol by continuous hot percolation with the help of soxhlet apparatus for 10hrs of time. On completion the extract was filtered and concentrated using rotary evaporator under reduced pressure and controlled temperature of 500C – 600 C. The concentrates were stored in the refrigerator for further use.

Experimental design
Adult Male Wistar rats of weighing 180-230 gms were used for this study. The inbred animals were procured from the animal house. They were housed five per cage under standard laboratory conditions at a room temperature at 22 ± 2^0 C with 12 hr light/dark cycle. The animals were acclimatized to laboratory conditions one week and provided with standard pellet chow and water *ad libitum*. Ethical committee clearance was obtained from IAEC of CPCSEA. (IAEC approval number: CPCSEA/IAEC/JLS/17/03/22/31)

Phytochemical qualitative analysis
The plant extracts were assessed for the existence of the phytochemical analysis[6]

Test for tannins
1ml of sample was taken, to that few drops of 0.1 % ferric chloride was added and observed for brownish green or blue black coloration.

Test for saponins
1 ml of sample was taken, to that 2 ml of water was added .The suspension was shaken in a graduated cylinder for 15 minutes. A layer of foam indicates the presence of saponins.

Test for flavonoids
1 ml of sample was taken, to that few drops of Sodium hydroxide solution was added. Formation of intense yellow colour, which becomes colourless on further addition of diluted hydrochloric acid, indicated the presence of flavonoid

Test for alkaloids
1 ml of sample was taken, to that few drops of dragandoff reagent was added. Prominent yellow precipitates indicate the test as positive.

Test for protein
1 ml of sample was taken, to that few drops of Millon's reagent was added. A white precipitate indicates the presence of Protein.

Test for steroids
1 ml of sample was taken, to those two drops of concentrated sulphuric acid was added and observed for brown colour.

Test fof anthraquinones
1 ml of sample was taken, to that aqueous ammonia was added and observed for change in colour. Pink, red, or violet colour in aqueous layer indicates the presence of anthraquinoness.

Test for phenol
1 ml of sample was taken, to that 3 ml of 10% lead acetate solution is added a bulky white precipitate indicates the presence of phenolic compounds.

Acute toxicity studies
Acute oral toxicity study was performed as per CPCSEA guidelines (acute toxic class method). The group of six animals were kept fasting for overnight and provided only with water, after which the extracts were administered orally at 5mg/kg body weight by gastric intubations and observed for 14 days. In case if the mortality was observed in two out of three animals, then the dose administered would be assigned as toxic dose. If mortality was observed in one animal, then the same dose would be repeated again to confirm the toxic dose. If mortality was not observed, the procedure would be repeated for higher doses such as 250, 500, 1000 and 2000 mg/kg body weight.[7]

Procedure
Adult male wistar albino rats weighed 180- 230gms were used for the study. The starting dose AE Was 2000mg/kg body weight p.o. Most of the crude extracts possess LD50 value more than 2000 mg/kg, p.o. so the starting dose which used was 2000mg/g p.o. Food was withheld for a further 3-4 hrs after administration (p.o) of drugs and observed for the signs of toxicity.

Body weights of rats before and after administration were observed for morbidity and mortality. Any changes in skin, fur, eyes, mucous membrane, respiratory, circulatory, autonomic & central nervous system, motor activity and behaviour pattern were observed and also sign of tremors, convulsion, salivation, diarrhoea, lethargy, sleep and coma were noted.

Induction of diabetes in experimental animals
Animals were allowed to fast for 12 h and were administered freshly prepared streptozotocin (STZ) at the concentration of 55 mg/kg bodyweight, i.p. in 0.1 mol/L cold citrate buffer, pH 4.5. The STZ-treated animals were allowed to drink 5% glucose solution overnight to overcome drug-induced hypoglycemia. Rats which were having persistent glycosuria and hyperglycaemia with a fasting blood glucose >250 mg/dL on the third day after the STZ injection were considered diabetic and which were used for further experimentation.[8]

Experimental design
The animals were divided into 5 groups each constituting 6 rats. Group I were normal rats received water, Group II were STZ (55 mg/kg b.w., i.p) induced diabetic rats which acts as diabetic control group. Group III STZ (55 mg/kg b.w., i.p) induced diabetic rats were treated with Glibenclamide 5mg/kg b.w/p.o Group IV STZ (55 mg/kg b.w., i.p) induced diabetic rats were treated with EEAE 200mg/kg b.w/ p.o Group V STZ (55 mg/kg b.w., i.p) induced diabetic rats were treated with EEAE 400mg/kg b w/p.o for 21 days.[9]

Fasting blood glucose levels was measured before the administration of extracts. The blood glucose levels were checked on 0th, 7th, 14th, and 21st day of the treatment period. Blood was collected from snipping of the rat tail.

Blood glucose levels were measured by using the glucose oxidase peroxidase reactive strips and a glucometer

Biochemical parameter studies

At the last day animal was sacrificed by decapitation, blood samples were collected and serum was separated using centrifuge to study the biochemical parameters. The estimation of protein was carried out using the method of Lowry.[10] The extraction of serum lipids were carried out by the method of Folch[11] and the serum cholesterol estimation was carried out by the method of Zlatkis[12] Serum triglycerides were estimated by the method of Foster and Dunn and HDL cholesterol was estimated by the method of Burstein.[13] The VLDL cholesterol was evaluated using the formula, TG/5 mg/dl. The serum LDL cholesterol was estimated by the method of Friedwald[14] SGOT and SGPT were measured by the method of Reitman and Frankel (Colorimetric method) the plasma creatinine was measured by Jaffe's method Serum urea was measured by the diacetyl monoxime method and Histopathology studies of liver and pancreas were carried out by using standard procedure.

Histopathology

At the end of the study, all the animals were sacrifices under light ether anesthesia. The rats were sacrificed by decapitation and blood samples were collected by bleeding of retro- orbitol plexus using micro capillary technique from all the groups of overnight fasted rats and serum was separated to study the biochemical parameters. The relevant organs like pancreas, liver and kidney were removed and dissected out and washed with ice-cold saline. The organs were preserved in 10% formalin solution for histopathological studies.

Statistical analysis

The data were expressed as mean ± standard error (SEM). The significance of differences among the groups was assessed using one way analysis of variance (ANOVA). The test followed by Dunnet's test p values lees than 0.05 were considered as significance.

RESULTS

Preliminary phytochemical analysis of ethanolic extract of andrographis elongata (EEAE)

Table 1: Phytochemical screening of EEAE.

Table: The Phytochemical studies	Sample
Tannins	+
Saponins	-
Flavonoids	+
Alkaloids	+
Proteins	+
Steroids	+
Anthroquinones	-
Phenol	+

The result of preliminary phytochemical analysis of Ethanolic extract of *Andrographis elongata* (EEAE) showed presence of various phytochemical constituents such as, flavonoids, alkaloids, tannins, proteins, steroids and phenol with absence of saponins and anthroquinones. The results were shown in **Table-1**

Acute oral toxicity study

Table 2: Acute oral toxicity studies of EEAE (OECD 423 guideline).

Si. No.	Treatment group	Dose	Weight of animalin gms		Signs of toxicity	Onset of toxicity	Reversible or irreversible	Duration
			Beforetest	Aftertest				
1.	EEAE	2g/kg	200	210	No signs of toxicity	Nil	Nil	14 days
2.	EEAE	2g/kg	180	195	No signs of toxicity	Nil	Nil	14 days
3.	EEAE	24g/kg	190	200	No signs of toxicity	Nil	Nil	14 days

Acute oral toxicity study was performed as per CPCSEA guidelines (acute toxic class method).The group of six animals were kept fasting for overnight and provided only with water, after which the extracts were administered orally at 2mg/kg body weight by gastric intubations and observed for 14 days. If mortality was observed in two out of three animals, then the dose administered was assigned as toxic dose. If mortality was observed in one animal, then the samedose was repeated again to confirm the toxic dose. If mortality was not observed, the procedurewas repeated for higher doses such as 250, 500, 1000 and 2000 mg/kg body weight. The results were shown in **Table-2.**

Effect of EEAE on body weight of STZ induced diabetic rats

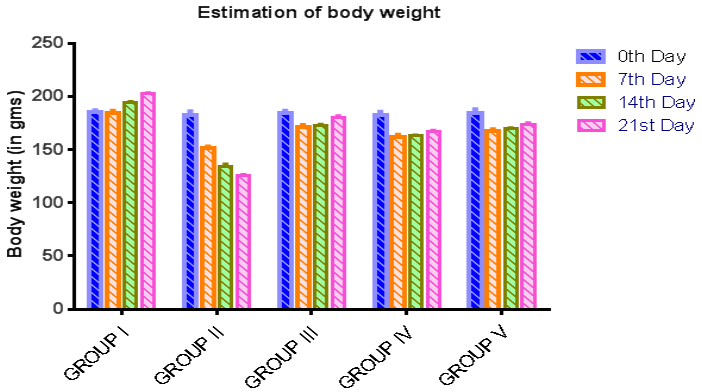
Table 3: Effect of EEAE on body weight of STZ induced diabetic rats.

Group	Body weight (gm)			
	Day – 0	Day – 7	Day – 14	Day – 21
I	185.2±1.930	184.2±2.271	194.5±0.7548	202.3±1.173
II	182.2±4.010	151.5±1.482 a***	134.5±1.988 a***	125.7±0.892 a***
III	182.34±2.186	171.2±2.012 a***b***	172.5±1.222 a***b***	180.0±1.780 a***b***
IV	182.12±3.615	161.7±2.236 ns a***b	162.8±0.9458 a***b***	167.2±0.938 a***b***
V	184.8±3.137	167.3±1.914 a***b***	169.8±0.9098 a***b***	173.8±1.337 a***b***

- Values are expressed as mean ± SEM of 6 animals.
- Statistical Significance test for comparison was done by one way ANOVA followed by Dunnets 't' test. Where *p< 0.05, **p< 0.01, ***P<0.001, ns-non significant.

Comparisons were made between the following:

- a - Group I vs. II,III,IV and V, b - Group II vs.III, IV, and V.



Histogram 1: Effect of EEAE on body weight.

It was found that the body weight was decreased significantly (p<0.001) when the comparison was made between group I with group II, group III, group IV and group V.

The bodyweight in group II was compared with group III, group IV and group V were increased significantly (p<0.001). The results were shown in **(Table-3) (Histogram-1)**

Effect of EEAE on blood glucose level of STZ induced diabetic rats

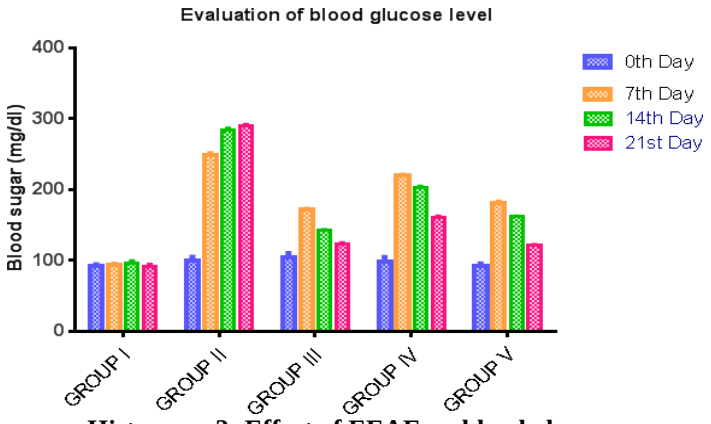
Table 4: Effect of EEAE on blood glucose level in STZ induced diabeticrats.

Group	Blood glucose (mg/dl)			
	Day – 0	Day – 7	Day – 14	Day – 21
I	91.35±3.130	93.50±1.660	95.83±3.646	91.33±2.996
II	100.178±4.649	249.07±1.922a a***	284.2±2.110 a***	290.7±1.510 a***
III	104.216±5.890	171.01±1.549 a***b***	141.89±1.461 a*** b***	122.795±1.783 a*** b***
IV	98.03±6.260	219.159±1.497 a***b***	202.53±2.057 a***b***	160.7±1.515 a***b***
V	92.131±3.170	181.371±1.438 a***b***	161.26±1.316 a***b***	121.049±1.150 a**b***

- Values are expressed as mean ± SEM of 6 animals.
- Statistical Significance test for comparison was done by one way ANOVA followed by Dunnets 't' test. Where *p< 0.05, **p< 0.01, ***P<0.001, ns-non significant.

Comparisons were made between the following

- a - Group I vs. II,III,IV and V, b - Group II vs.III, IV, and V.



Histogram 2: Effect of EEAE on blood glucose.

The blood glucose levels were compared between group I with group II, group III, group IV and group V and it was found that blood glucose levels were significantly increased ($p<0.001$).

The blood glucose levels in group II was compared with group III, group IV and group V were significantly ($p<0.001$) decreased. The results were shown in (Table-4) (Histogram-2)

Effect of EEAE on serum cholesterol level of STZ induced diabetic rats

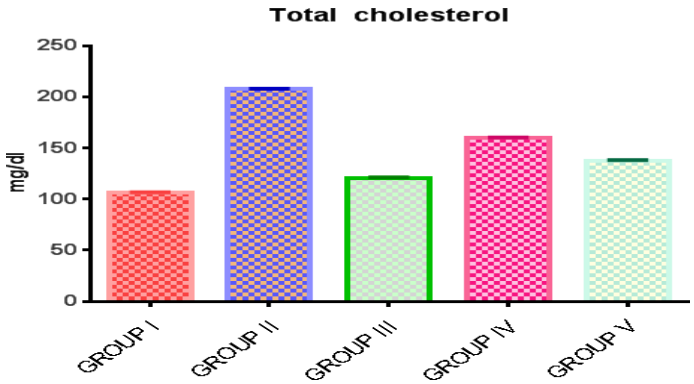
Table 5: Effect of EEAE on total cholesterol, Triglycerides, HDL, LDL,VLDL.

Groups	Treatment	Total cholesterol (mg/dl)	Triglycerides (mg/dl)	HDL (mg/dl)	LDL (mg/dl)	VLDL (mg/dl)
I	Control	106.3±0.352	86.4±0.38	61.03±0.37	41.4±0.48	18.69±0.49
II	Diabeticcontrol 55mg stz	207.6±0.319 a***	170.2±0.44 a***	34.56±0.46 a***	139.43±0.74 a***	40.17±0.61 a***
III	STZ+ Glibenclamide	120.7±0.576 a***b***	92.1±0.49 a***b***	56.71±0.69 a**b***	86.59±0.42 a**b***	26.69±0.37 a***b***
IV	STZ+EEAE 200 mg	159.83±0.29 a***b***	129.4±0.29 a***b***	42.03±0.37 a***b***	113.21±0.49 a***b***	30.46±0.29 a***b***
V	STZ+EEAE 400 mg	137.783±0.390 a***b***	100.1±0.18 a***b***	53.21±0.53 a***b***	92.84±0.51 a***b***	24.84±0.24 a***b***

- Values are expressed as mean ± SEM of 6 animals.
- Statistical Significance test for comparison was done by one way ANOVA followed by Dunnets 't' test. Where *p< 0.05, **p< 0.01, ***P<0.001, ns-non significant.

Comparisons were made between the following

- a - Group I vs. II,III,IV and V, b - Group II vs.III, IV, and V.

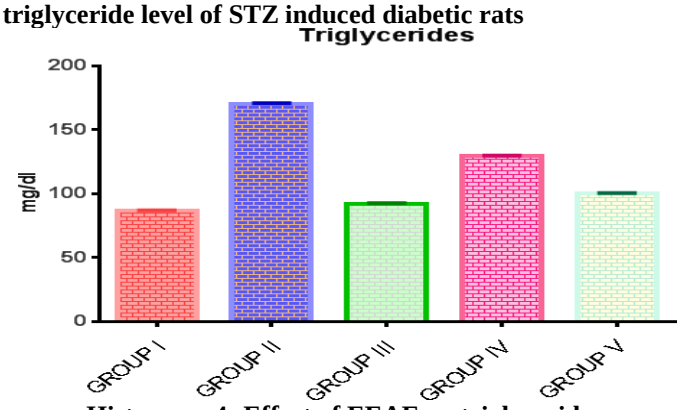


Histogram 3: Effect of EEAE on total cholesterol.

The serum cholestrol levels were compared between group I with group II, group III, group IV and group V and it was found that serum cholesterol levels were significantly increased($p<0.001$).

The serum creatinine level in group II was compared with group III, group IV and group V were decreased significantly ($p<0.001$). The results were shown in **(Table-5) (Histogram-3)**

Effect of EEAE on serum triglyceride level of STZ induced diabetic rats

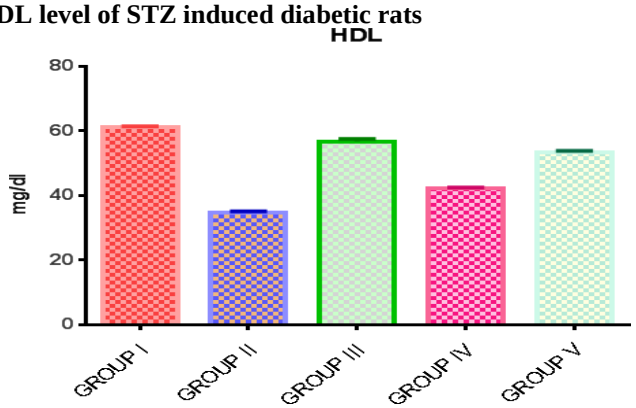


Histogram 4: Effect of EEAE on triglycerides.

The serum triglycerides levels were compared between group I with group II, group III, group IV and group V and it was found that serum triglycerides levels were significantly increased ($p<0.001$).

The serum triglyceride level in group II was compared with group III, group IV and group V ($p<0.001$) were decreased significantly. The results were shown in **(Table-5) (Histogram-4).**

Effect of EEAE on serum HDL level of STZ induced diabetic rats

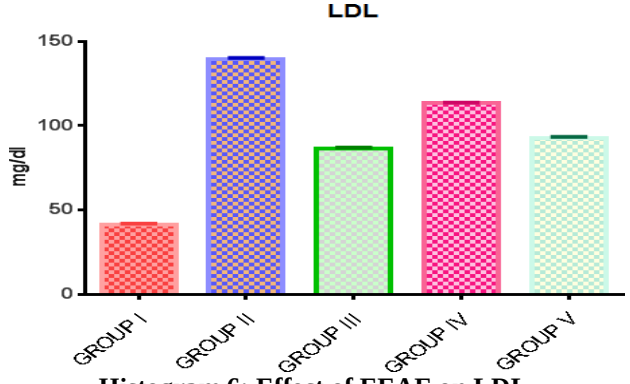


Histogram 5: Effect of EEAE on HDL.

The serum HDL levels were compared between group I with group II, group III, groupIV and group V and it was found that serum HDL levels were significantly decreased ($p<0.001$).

The HDL level in group II was compared with group III group IV and group V ($p<0.001$) increased significantly. The results were shown in **(Table-5) (Histogram-5).**

Effect of EEAE on serum LDL level of STZ induced diabetic rats

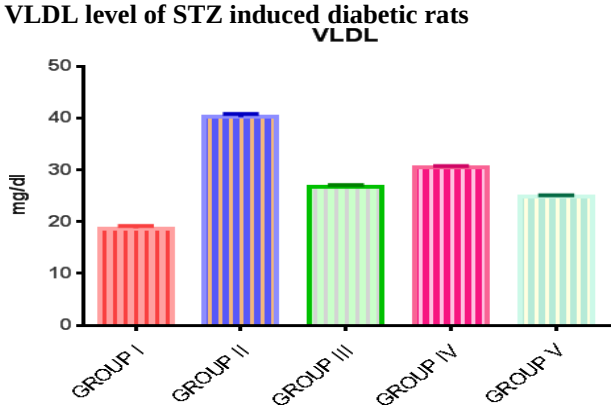


Histogram 6: Effect of EEAE on LDL.

The serum LDL levels were compared between group I with group II, group III, groupIV and group V and it was found that serum LDL levels were significantly increased ($p<0.001$).

The serum LDL level in group II was compared with group III group IV and group V ($p<0.001$) were significantly decreased. The results were shown in **(Table-5) (Histogram-6).**

7.9 Effect of EEAE on serum VLDL level of STZ induced diabetic rats



Histogram 7: Effect of EEAE on VLDL.

The serum VLDL levels were compared between group I with group II, group III, group IV and group V and it was found that serum VLDL levels were significantly increased (p<0.001).he serum VLDL level in group II was compared with group III, group IV and group V were significantly decreased (p<0.001). The results were shown in **(Table-5) (Histogram-7).**

Effect of EEAE on serum total protein level of STZ induced diabetic rats

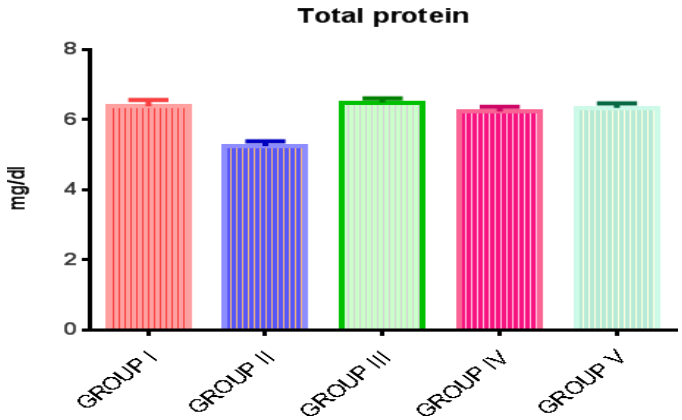
Table 6: Effect of EEAE on Total protein in STZ induced diabetic rats.

Groups	Treatment	Total protein (mg/dl)
I	Control	6.38±0.1767
II	STZ (55mg/kg b.w., i.p) induced diabetic rats	5.24±0.1344 a**
III	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with glibenclamide (5mg/kg b.w., p.o)	6.48±0.1186 a^{ns} b***
IV	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with EEAE (200mg/kg b.w., p.o)	6.23±0.1271 a^{ns} b**
V	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with EEAE (400mg/kg b.w., p.o)	6.33±0.1308 a^{ns} b**

- Values are expressed as mean ± SEM of 6 animals.
- Statistical Significance test for comparison was done by one way ANOVA followed by Dunnets 't' test. Where *p< 0.05, **p< 0.01, ***P<0.001, ns-non significant.

Comparisons were made between the following:

- a - Group I vs. II,III,IV and V, b - Group II vs.III, IV, and V.



Histogram 8: Effect of EEAE on Total Protein.

The serum total protein level in group I was compared with group II (p<0.01), group III(ns), group IV (ns) and group V (ns) were increased significantly.

The serum total protein level in group II was compared with group III, (0.001) group IV and group V (p<0.01) were decreased significantly. The results were shown in **(Table-6) (Histogram-8).**

Effect of EEAE on serum creatinine level of STZ induced diabetic rats

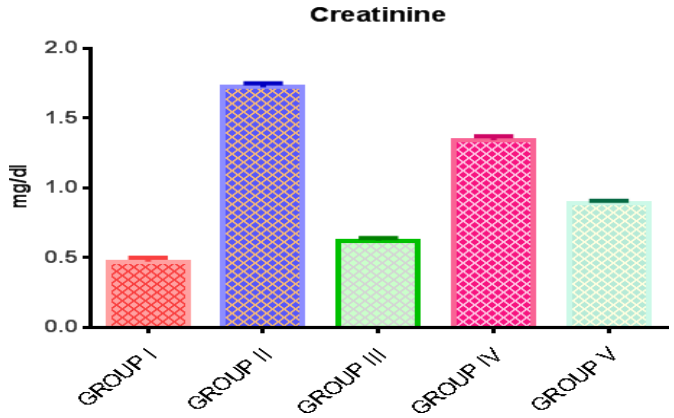
Table 7: Effect of EEAE on Creatinine in STZ induced diabetic rats.

Groups	Treatment	Creatinine (mg/dl)
I	Control	0.47±0.0281
II	STZ (55mg/kg b.w., i.p) induced diabetic rats	1.72±0.0277 a***
III	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with glibenclamide (5mg/kg b.w., p.o)	0.62±0.0185 a***b***
IV	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with EEAE (200mg/kg b.w., p.o)	1.34±0.0296 a***b***
V	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with EEAE (400mg/kg b.w., p.o)	0.89±0.0170 a***b***

- Values are expressed as mean ± SEM of 6 animals.
- Statistical Significance test for comparison was done by one way ANOVA followed by Dunnets 't' test. Where *p< 0.05, **p< 0.01, ***P<0.001, ns-non significant.

Comparisons were made between the following:

- a - Group I vs. II,III,IV and V, b - Group II vs.III, IV, and V.



Histogram 9: Effect of EEAE on Creatinine.

The serum creatinine level in group I was compared with group II group III group IV and group V (p<0.001) and it was found that the levels were increased significantly.

The serum creatinine level in group II was compared with group III, group IV and groupV (p<0.001) were decreased significantly. The results were shown in **(Table-7) (Histogram-9).**

Effect of EEAE on SGOT level of STZ induced diabetic rats

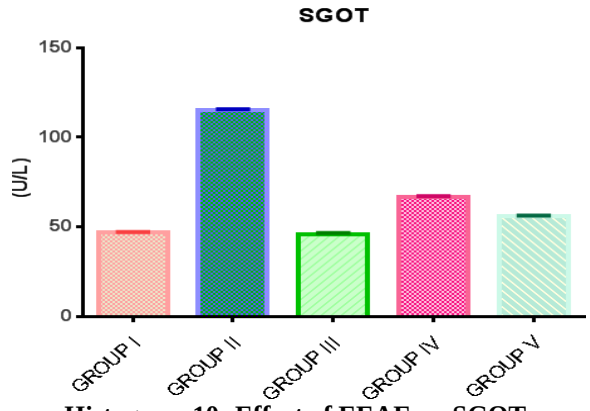
Table 8: Effect of EEAE on SGOT in liver tissue of STZ induced diabetic rats.

Groups	Treatment	SGOT (U/L)
I	Control	47.01±0.12
II	STZ (55mg/kg b.w., i.p) induced diabetic rats	115.03±0.64 a***
III	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with glibenclamide (5mg/kg b.w., p.o)	45.86±0.58 a***b***
IV	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with EEAE (200mg/kg b.w., p.o)	66.83±0.29 a***b***
V	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with EEAE (400mg/kg b.w., p.o)	55.86±0.36 a***b***

- Values are expressed as mean ± SEM of 6 animals.
- Statistical Significance test for comparison was done by one way ANOVA followed by Dunnets 't' test. Where *p< 0.05, **p< 0.01, ***P<0.001, ns-non significant.

Comparisons were made between the following:

- a - Group I vs. II,III,IV and V, b - Group II vs.III, IV, and V.



Histogram 10: Effect of EEAE on SGOT.

The SGOT level in group I was compared with group II group III group IV and group V ($p<0.001$) and it was found that the levels were increased significantly.

The SGOT level in group II was compared with group III, group IV and group V were decreased significantly ($p<0.001$). The results were shown in **(Table-8) (Histogram-10).**

Effect of EEAE on SGPT level of STZ induced diabetic rats

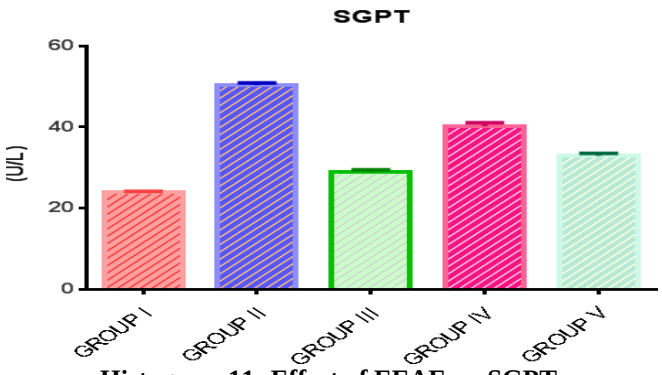
Table 9: Effect of EEAE on SGPT in liver tissue of STZ induced diabeticrats.

Groups	Treatment	SGPT (U/L)
I	Control	24.01±0.12
II	STZ (55mg/kg b.w., i.p) induced diabetic rats	50.29±0.54 a***
III	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with glibenclamide (5mg/kg b.w., p.o)	28.86±0.58 a***b***
IV	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with EEAE (200mg/kg b.w., p.o)	40.13±0.89 a***b***
V	STZ (55mg/kg b.w., i.p) induced diabetic rats treated with EEAE (400mg/kg b.w., p.o)	32.86±0.66 a***b***

- Values are expressed as mean ± SEM of 6 animals.
- Statistical Significance test for comparison was done by one way ANOVA followed by Dunnets 't' test. Where *p< 0.05, **p< 0.01, ***P<0.001, ns-non significant.

Comparisons were made between the following:

- a - Group I vs. II,III,IV and V, b - Group II vs.III, IV, and V.



Histogram 11: Effect of EEAE on SGPT.

The SGPT level in group I was compared with group II group III group IV and group V ($p<0.001$) and it was found that the levels were increased significantly.

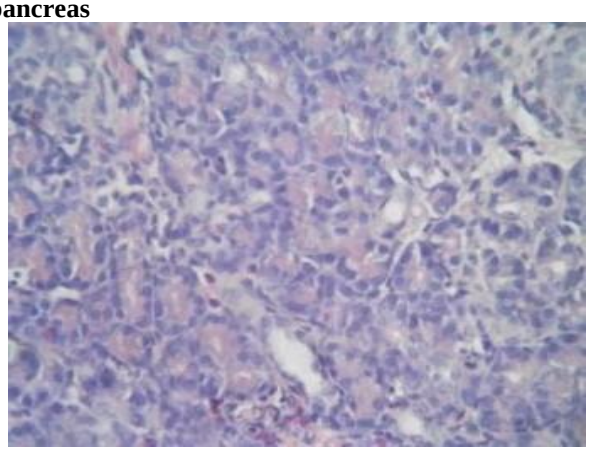
The SGPT level in group II was compared with group III, group IV and group V weredecreased significantly ($p<0.001$). The results were shown in **(Table-9) (Histogram-11).**

Histopathology of pancreas

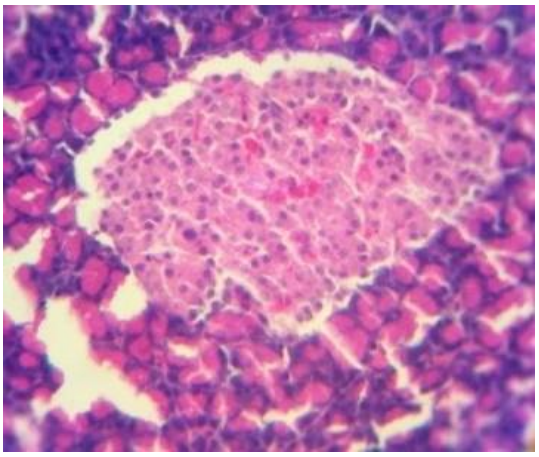
The histopathology of rat pancreas of control groups showed normal acini and islets whereas diabetic control groups showed damaged and atrophy islets with acini. Diabetic animal treated with glibenclamide (5mg/kg b.w/p.o) has showed preserved normal islets in pancreas, whereas EEAE 200mg/kg/p.o treated animals has showed small pancreatic islet and EEAE 400mg/kg/p.o

treated animals showed hyperplastic.

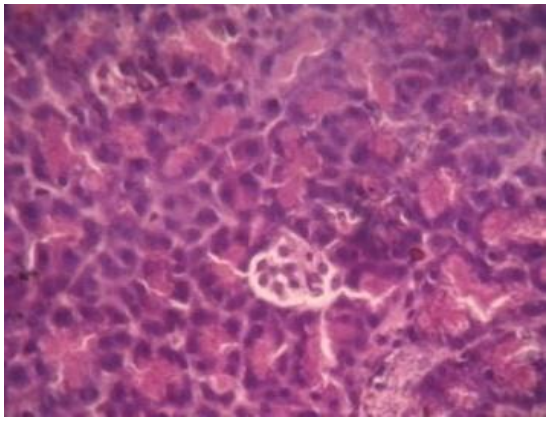
Histopathological analysis of pancreas



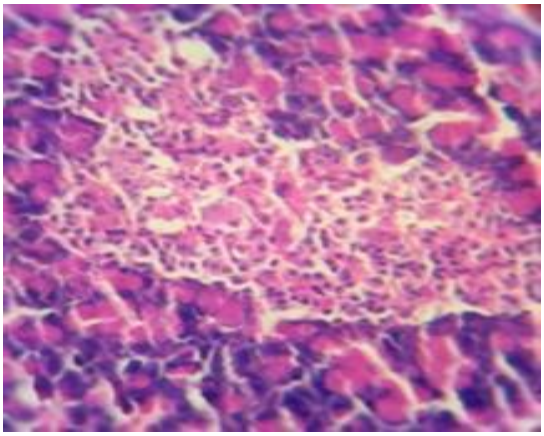
Histopathology of Pancreas- Group-I



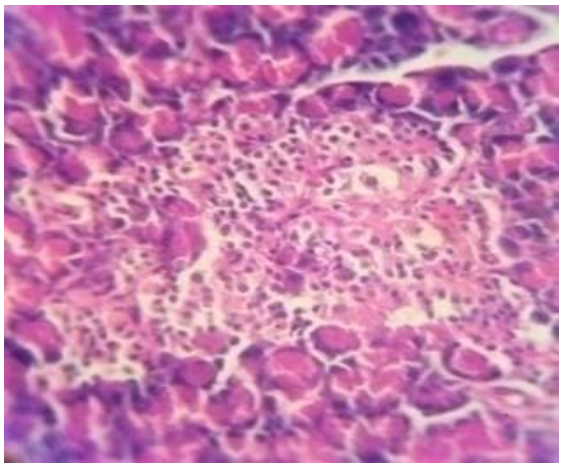
Histopathology of Pancreas- Group-II



Histopathology of Pancreas- Group-III



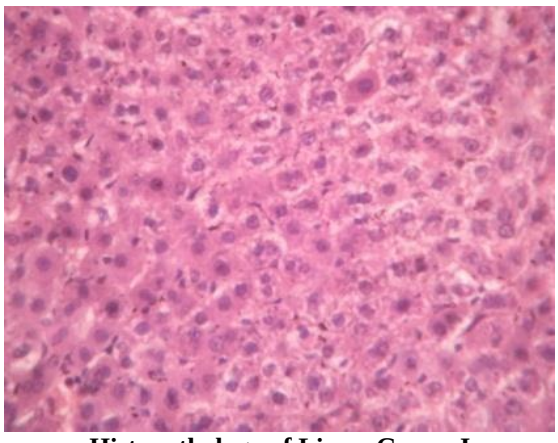
Histopathology of Pancreas- Group-IV



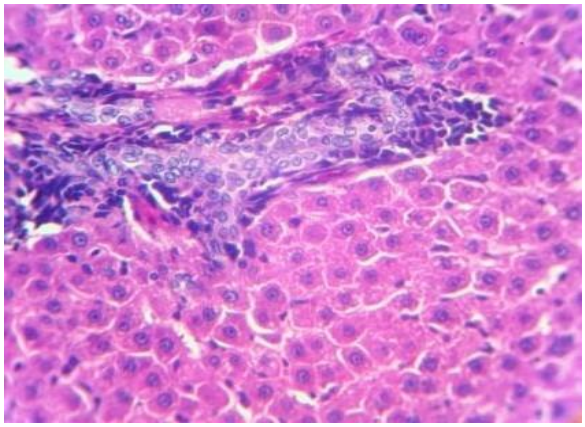
Histopathology of Pancreas- Group-V

Histopathology of Liver

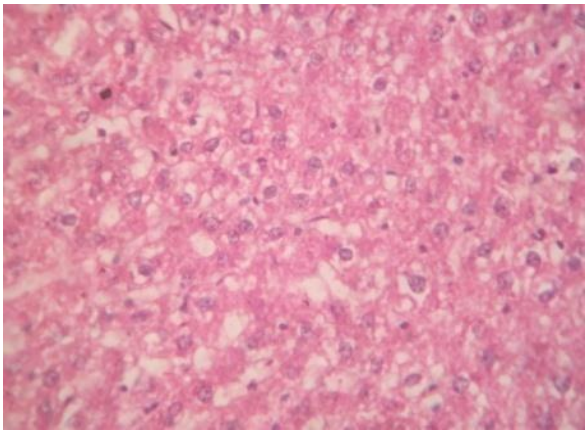
Histopathological examinations of diabetic animals showed centrilobular necrosis accompanied by fatty changes and ballooning degeneration which were observed in the remaining hepatocytes in the liver of rats treated with STZ (55mg/kg b.w/p.o) were much of intensity and which were recovered with the treatments using EEAE.



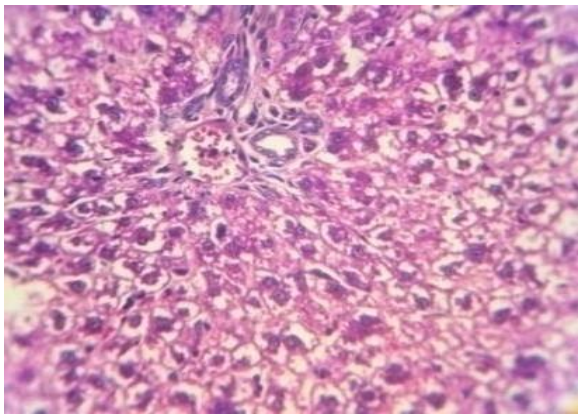
Histopathology of Liver- Group-I



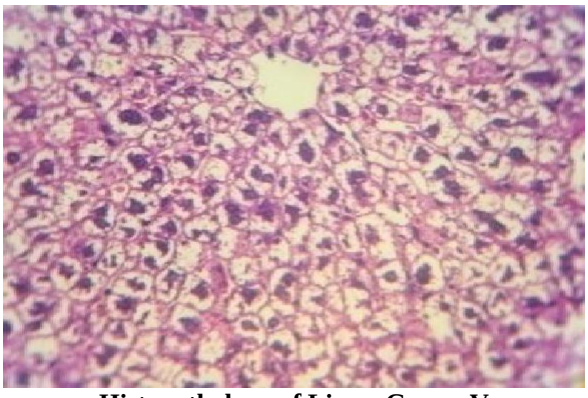
Histopathology of Liver- Group-II



Histopathology of Liver- Group-III



Histopathology of Liver- Group-IV



Histopathology of Liver- Group-V

DISCUSSION

The ethanolic extract from whole plant of *Andrographis elongata* were subjected to preliminary phytochemical analysis which shown presence of flavonoids, alkaloids, Glycosides, tannins, proteins, steroids and phenol with absence of saponins and anthroquinones.

Acute oral toxicity studies of EEAE did not produce any mortality or signs of toxicity at the dose of 2000 mg/kg b.w/p.o, in experimental rats.

The anti-hyperglycemic effects of the plants is due to their ability to restore the functionof pancreatic tissues by causing an increase in insulin output or inhibit the intestinal absorption of glucose or to the facilitation of metabolites in insulin dependent processes. Hence, treatmentwith herbal drugs has an effect on protecting b cells and smoothing out fluctuation in glucose levels The present study evalulation of anti-diabetic activity of leaves of *Andrographis elongata* STZ induced diabetic rats.

Experimental induction of hyperglycemia with STZ is associated with the characteristic loss of body weight which is due to loss or degradation of structural proteins it leads to increasedmuscle wasting and due to loss of tissue protein, as the structural proteins are known to contribute to body weight. Diabetic rats treated with glibenclamide and EEAE showed increasedbody weight when compared to untreated diabetic animals. It may be due to increased insulin secretion and glycemic control of EEAE.

Reduced glucose transport or absorption from the gut, extra pancreatic action probably by stimulation of glucose utilization in peripheral tissues, increase in glycogenic or glycolytic enzyme activities in peripheral tissues, decrease in the secretion of counter-regulatory hormones like glucagon, growth hormones are the possible mechanisms involved with suppressing blood glucose levels. The glibenclamide, stimulating insulin secretion from pancreatic β cells principally by inhibiting ATP sensitive KATP channels in the plasma membrane and decreases the blood glucose level. Blood glucose level decreased significantly in glibenclamide and EEAE treated diabetic rats and the histopathology of pancreas showed normal islets in pancreas with normal anatomy compared with normal rats which may be due to the anti-diabetic activity.

Hyperglycaemia is accompanied with dyslipidemia under normal circumstances; insulin activates the enzyme lipoprotein lipase, which hydrolyses triglycerides. However, in diabetic state lipoprotein lipase is not activated due to insulin deficiency, resulting in hyper triglyceridemia, and insulin deficiency is also associated with hyper cholesterolemia due to metabolic abnormalities. The dyslipidemia is characterized by increase in TC, LDL, VLDL, TGand fall in HDL which is observed in STZ induced diabetic rats. The diabetic rats treated with glibenclamide and EEAE showed reduced severity of dyslipidemia with decrease in TC, LDL, VLDL, TG and increase in HDL.

Both SGOT and SGPT enzyme levels get elevated during liver damage which is more in diabetic rats[75]. The diabetic rats treated with glibenclamide and EEAE reduced the SGOT and SGPT level. The liver histopathology of STZ induced diabetic rats showed centrilobular necrosis accompanied by fatty changes and ballooning degeneration in the hepatocytes treatment with EEAE reversed in diabetic rats treated with glibenclamide and EEAE which indicates that the liver damage is reduced in EEAE treated group.

The diabetic hyperglycaemia induces elevation of the serum levels of creatinine which are significant markers of renal dysfunction, The treatment of EEAE in rats showed marked decrease in serum creatinine levels in diabetic animals.

CONCLUSION

The anti-diabetic activity of leaves of *Andrographis elongata* is evidenced byblood glucose level, estimation of lipid profile activity of *Andrographis elongata* and the evidentreduction in SGOT, SGPT in liver and creatinine in serum also proves that the *Andrographis elongata* reduced the Pancreas, liver damage which is common in diabetes.Thus, it may be concluded that *Andrographis elongata* produced significant antidiabetic activity in streptozotocin induced diabetic rats. The efficacy of the *Andrographis elongata* was comparable to that of Glibenclamide.

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